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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF MAILING

I hereby certify that this **INFORMATION DISCLOSURE STATEMENT** and documents submitted therewith are being deposited with the United States Postal Service as first class mail, postage prepaid thereon, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Mancy Malsich

Applicant: Nicolaou, et al.

Serial No.: 10/634,537

Filed: August 4, 2003

For: ANALOGS OF EPOTHILONE

Applicant: Nicolaou, et al.

Confirmation No.: 6050

Examiner: L. Stockton

Our Ref.: TSRI 904.1

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

In recognition of their continuing duty to disclose pursuant to 37 CFR §1.56, Applicants hereby submit the present Information Disclosure Statement and accompanying PTO Form 1449 in compliance therewith.

Applicants understand that the interpretation given to each reference may differ from one individual to another. The PTO is therefore encouraged to independently examine the disclosed references. While the references provided in this Information Disclosure Statement may be material pursuant to 37 CFR \$1.56, it shall not be construed to be an admission that the cited information is, or is considered to be, material to patentability unless specifically designated as such.

Applicants are filing the present statement pursuant to 37 CFR \$1.97(d). The statement is accompanied by a check in the amount of \$180.00 as payment of the fee set forth in 37 CFR \$1.17(p) in accordance with 37 CFR \$1.97(d)(2).

Also, in accordance with 37 CFR §1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or, that if made, any search was complete or exhaustive, or that no other material information as defined in 37 CFR §1.56 exists.

Respectfully submitted,

April 19, 2005

Donald G. Lewis, Reg. No. 28,636

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| | | OT | HED DOCUMENTS (In | aluding Author Title Date | Dartinant Dagge | | | | | | |
| | 1 | OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages) Souto, et al., "New Fluorescent Water-Soluble Taxol Derivatives", <u>Angew. Chem. Int. Ed. Engl. 34</u> : 2710-2712 (1995) | | | | | | | | | |
| | 2 | Nicolaou, et al., "The Olefin Metathesis Approach to Epothilone A and Its Analogues", J. Am. Chem. Soc. 119: 7960-7973 (1997) | | | | | | | | | |
| | 3 | Nicolaou, et al., "Total Syntheses of Epothilones A and B via a Macrolactonization-Based Strategy", J. Am. Chem. Soc. 119: 7974-7991 (1997) | | | | | | | | | |
| | 4 | Nicolaou, et al., "Designed Epothilones: Combinatorial Synthesis, Tubulin Assembly Properties, and Cytotoxic Action against Taxol-Resistant Tumor Cells", Angew. Chem. Int. Ed. Engl. 36: 2097-2103 (1997) | | | | | | | | | |
| | 5 | Nicolaou, et al., "Total Synthesis of Epothilone E and Analogues with Modified Side Chains through the Stille Coupling Reaction", Angew. Chem. Int. Ed. Engl. 37: 84-87 (1998) | | | | | | | | | |
| | 6 | Nicolaou, et al., "Chemical Biology of Epothilones", Angew. Chem. Int. Ed. Engl. 37: 2015-2045 (1998) | | | | | | | | | |
| | 7 | Nicolaou, et al., "Total Synthesis of Epothilone E and Related Side-chain Modified Analogues via a Stille Coupling Based Strategy", Bioorg. Med. Chem. 7: 665-697 (1999) | | | | | | | | | |
| | 8 | Giannakakou, et al., "A common pharmacophore for epothilone and taxanes: Molecular basis for drug resistance conferred by tubulin mutations in human cancer cells", <u>Proc. Natl. Acad. Sci. USA 97</u> : 2904-2909 (2000) | | | | | | | | | |
| | 9 | Johnson, et al., "Synthesis, Structure Proof, and Biological Activity of Epothilone Cyclopropanes", Org. Lett. 2: 1537-1540(2000) | | | | | | | | | |
| | 10 | Nicolaou, et al., "Chemical | Nicolaou, et al., "Chemical synthesis and biological properties of pyridine epothilones", Chem. Biol. 7: 593-599 (2000) | | | | | | | | |
| | 11 | Nicolaou, et al., "Total Synthesis of 16-Desmethylepothilone B, Epothilone B ₁₀ , Epothilone F, and Related Side Chain Modified Epothilone B Analogues", Chem. Eur. J. 6: 2783-2800 (2000) | | | | | | | | | |
| | 12 | Nicolaou, et al., "Synthesis and Biological Evaluation of 12,13-Cyclopropyl and 12,13-Cyclobutyl Epothilones", ChemBioChem 2: 69-75 (2001) | | | | | | | | | |
| | 13 | Sinha, et al., "Synthesis of Epothilone Analogues by Antibody-Catalyzed Resolution of Thiazole Aldol Synthons on a Multigram Scale. Biological Consequences of C-13 Alkylation of Epothilones", ChemBioChem 2 : 656-665 (2001) | | | | | | | | | |
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| FORM PTO-14 | 49 U.S. DEPARTMENT OF O PATENT AND TRADEMA | | | | ATTY DOCKET NO. TSRI 904.1 | | SERIAL NO. 10/634,537 | | | | |
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| | | OTHER DOCUMENTS (Incli | uding Author, Title, Date | e, Pertinent Pages | 3) | | | | | | |
| | | Nicolaou, et al., "Recent developments in the chemistry, biology and medicine of the epothilones", <u>Chem. Commun.</u> : 1523-1535 (2001) | | | | | | | | | |
| | | Andreu, et al., "The Interaction of Baccatin III with the Taxol Binding Site of Microtubules Determined by a Homogenous Assay with Fluorescent Taxoid", <u>Biochemistry</u> 40: 11975-11984 (2001) | | | | | | | | | |
| Nicolaou, et al., "Chemical Synthesis and Biological Evaluation of <i>cis</i> - and <i>trans</i> -12,13-Cyclopropyl and 12, Epothilones and Related Pyridine Side Chain Analogues", <u>J. Am. Chem. Soc. 123</u> : 9313-9323 (2001) | | | | | | | | | | | |
| | Nicolaou, et al., "Chem analogues", <u>Tetrahedro</u> | Nicolaou, et al., "Chemical synthesis and biological evaluation of novel epothilone B and <i>trans</i> -12,13-cyclopropyl epothilone B analogues", <u>Tetrahedron 58</u> : 6413-6432 (2002) | | | | | | | | | |
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